# Pneumococcal 13-valent Conjugate Vaccine (Prevnar 13®)

**National Drug Monograph**
**December 2012**
**VA Pharmacy Benefits Management Services,**
**Medical Advisory Panel, and VISN Pharmacist Executives**

*The purpose of VA PBM Services drug monographs is to provide a comprehensive drug review for making formulary decisions. These documents will be updated when new clinical data warrant additional formulary discussion. Documents will be placed in the Archive section when the information is deemed to be no longer current.*

## Executive Summary:

- In adults 50 years of age and older, pneumococcal 13-valent conjugate vaccine (PCV13) is FDA approved for the prevention of pneumonia and invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. This indication is based on immunogenicity studies that evaluated antibody response of PCV13 compared to pneumococcal 23-valent polysaccharide vaccine (PPSV23). As part of the FDA accelerated approval process utilized for PCV13, the pharmaceutical company is currently conducting a clinical trial to evaluate the clinical benefit of PCV13 in persons who are pneumococcal-vaccine naïve.
- Two pivotal clinical trials evaluated the immunogenicity and safety of PCV13 compared to PPSV23 in different patient populations (i.e., pneumococcal-naïve and –experienced adults). Both trials demonstrated the non-inferiority of PCV13 to PPSV23 for the 12 serotypes contained in both vaccines. PCV13 was generally well-tolerated, and according to ACIP, similar serious and common adverse reactions were seen between PCV13 and PPSV23 in adults.
- Due to the lack clinical outcomes data in adults coupled with unknown impact of routine vaccination with PCV13 in children on the serotypes causing pneumococcal disease in adults, ACIP is currently not recommending routine use of PCV13 in immunocompetent adults 50 years of age and older. However, due to the higher risk of pneumococcal disease in certain patient populations, ACIP is recommending the routine use of 13-valent pneumococcal conjugate vaccine for adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants. PCV13 should be administered to eligible adults in addition to the 23-valent pneumococcal polysaccharide vaccine.

## Introduction

The purposes of this monograph are to (1) evaluate the available evidence of safety, tolerability, efficacy, cost, and other pharmaceutical issues that would be relevant to evaluating this vaccine for possible addition to the VA National Formulary; (2) define its role in therapy; and (3) identify parameters for its rational use in the VA.

## Pharmacology/Pharmacokinetics [1-3]

Pneumococcal 13-valent conjugate vaccine is a sterile suspension of saccharides of the capsular antigens of *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, individually linked to nontoxic diphtheria CRM197 protein (adjuvant). In comparison, the PPSV23 contains all of the serotypes in PCV13, except for serotype 6A, which is unique to PCV13. In addition, PPSV23 contains 11 serotypes (i.e., 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, and 33F) that are not available in PCV13. PCV13 elicits a T-cell dependent immune response.

## FDA Approved Indication(s) [1]

In adults 50 years of age and older, PCV13 is indicated for the prevention of pneumonia and invasive disease caused by *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

- This indication is based on immune responses elicited by PCV13.
- There have been no controlled trials in adults demonstrating a decrease in invasive pneumococcal disease or pneumococcal pneumonia after vaccination with PCV13.
- PCV13 will not protect against disease caused by *S. pneumonia* serotypes that are not in the vaccine.
- The effectiveness of PCV13 administered less than 5 years after PPSV23 is not known.

## ACIP Recommendations[3-4]

Refer to the current ACIP recommendations for "Licensure of 13-valent Pneumococcal Conjugate Vaccine for Adults Aged 50 years and Older" (MMWR June 1, 2012; Vol. 61, No. 21) and "Use of the 13-valent Pneumococcal Conjugate Vaccine and 23-valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions" (MMWR October 12, 2012; Vol. 61, No 40); Summary provided in Table 1 and Table 2.

**Table 1. ACIP Recommendations for Pneumococcal Vaccination**

| | Immunocompetent Adults ≥ 50 Years of Age | Immunocompromised Adults ≥ 19 Years of Age |
|---|---|---|
| **PCV13** | • NOT recommended for routine use | • Recommended one time dose for immunocompromising conditions, functional/anatomic asplenia, CSF leaks, or cochlear implants (Refer to Table 2 below).<br>• This is in addition to the PPSV23 recommendations (i.e., PCV13 does not replace PPSV23 administration). |

| | Adults 19 – 64 Years of Age | Adults ≥ 65 Years of Age |
|---|---|---|
| **PPSV23** | • Recommended vaccination for adults at high risk at the time of diagnosis of the high-risk condition (Table 2).<br>• A one-time revaccination is recommended 5 years after the first dose for persons with functional/anatomic asplenia and immunocompromising conditions (Table 2). | • Recommended one time dose regardless of previous PPSV23 vaccination.<br>• A minimum interval of 5 years between PPSV23 doses should be maintained. |

**Table 2. ACIP Recommendations for Specific Conditions to Administer PCV13 and PPSV23***

| | | PCV13 | PPSV23 | |
|---|---|---|---|---|
| **Risk group** | **Underlying medical condition** | **Recommended** | **Recommended** | **Revaccination 5 yrs after first dose** |
| Immunocompetent persons | Chronic heart disease† | | ✓ | |
| | Chronic lung disease§ | | ✓ | |
| | Diabetes mellitus | | ✓ | |
| | Cerebrospinal fluid leak | ✓ | ✓ | |
| | Cochlear implant | ✓ | ✓ | |
| | Alcoholism | | ✓ | |
| | Chronic liver disease, cirrhosis | | ✓ | |
| | Cigarette smoking | | ✓ | |
| Persons with functional or anatomic asplenia | Sickle cell disease/other hemaglobinopathy | ✓ | ✓ | ✓ |
| | Congenital or acquired asplenia | ✓ | ✓ | ✓ |
| Immunocompromised persons | Congenital or acquired immunodeficiency¶ | ✓ | ✓ | ✓ |
| | Human immunodeficiency virus infection | ✓ | ✓ | ✓ |
| | Chronic renal failure | ✓ | ✓ | ✓ |
| | Nephrotic syndrome | ✓ | ✓ | ✓ |
| | Leukemia | ✓ | ✓ | ✓ |
| | Lymphoma | ✓ | ✓ | ✓ |
| | Hodgkin disease | ✓ | ✓ | ✓ |
| | Generalized malignancy | ✓ | ✓ | ✓ |
| | Iatrogenic immunosuppression** | ✓ | ✓ | ✓ |
| | Solid organ transplant | ✓ | ✓ | ✓ |
| | Multiple myeloma | ✓ | ✓ | ✓ |

* All adults aged ≥65 years should receive a dose of PPSV23, regardless of previous history of vaccination with pneumococcal vaccine.
† Including congestive heart failure and cardiomyopathies, excluding hypertension.
§ Including chronic obstructive pulmonary disease, emphysema, and asthma.
¶ Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).
** Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.

## Potential Off-label Uses [1-4]

This section is not intended to promote any off-label uses. Off-label use should be evidence-based. See VA PBM-MAP and Center for Medication Safety's Guidance on "Off-label" Prescribing (available on the VA PBM Intranet site only).

Refer to ACIP recommendations.

## Current VA National Formulary Alternatives

The PPSV23 is on the National Formulary without Criteria for Use; however, ACIP recommends use of PPSV23 in conjunction with PCV13 for specific conditions (Table 2).

## Dosage and Administration [1,4]

FDA indication for adults 50 years of age and older: Single administration of PCV13; the deltoid muscle of the upper arm is the preferred site for injection.

ACIP recommendations: Administer one dose of PCV13 in adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants. PCV13 should be administered to eligible adults in addition to the PPSV23. The scheduling of the PCV13 is dependent if the person is pneumococcal vaccine-naïve or has received previous vaccination with PPSV23

- **Pneumococcal vaccine-naïve persons.** ACIP recommends that adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, CSF leaks, or cochlear implants, and who have not previously received PCV13 or PPSV23, should receive a dose of PCV13 first, followed by a dose of PPSV23 at least 8 weeks later. Subsequent doses of PPSV23 should follow current PPSV23 recommendations for adults at high risk. Specifically, a second PPSV23 dose is recommended 5 years after the first PPSV23 dose for persons aged 19–64 years with functional or anatomic asplenia and for persons with immunocompromising conditions. Additionally, those who received PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years, or later if at least 5 years have elapsed since their previous PPSV23 dose.

- **Previous vaccination with PPSV23.** Adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, CSF leaks, or cochlear implants, who previously have received ≥1 doses of PPSV23 should be given a PCV13 dose ≥1 year after the last PPSV23 dose was received. For those who require additional doses of PPSV23, the first such dose should be given no sooner than 8 weeks after PCV13 and at least 5 years after the most recent dose of PPSV23. As stated above, a second PPSV23 dose is recommended 5 years after the first PPSV23 dose for persons aged 19–64 years with functional or anatomic asplenia and for persons with immunocompromising conditions. Additionally, those who received PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years, or later if at least 5 years have elapsed since their previous PPSV23 dose.

## Efficacy [1,3,5,6]

The immunogenicity of the PCV13 in adults was evaluated in five phase 3 clinical trials; two of these trials were considered pivotal for FDA approval and summarized below by CDC and in the Appendix. Neither of the two pivotal trials has been published in the literature with the exception of the CDC summary in the MMWR report entitled "Licensure of 13-valent Pneumococcal Conjugate Vaccine for Adults Aged 50 years and Older" (MMWR June 1, 2012; Vol. 61, No. 21).

### Efficacy Measures

- Antibody response elicited by PCV13 and PPSV23 measured by opsonophagocytic antibody (OPA) assay was utilized to measure vaccine effectiveness.
- OPA provides an in vitro measurement of the ability of serum antibodies to eliminate pneumococci by promoting complement-mediated phagocytosis and is believed to reflect relevant in vivo mechanisms of protection against pneumococcal disease. OPA titers are expressed as the reciprocal of the highest serum dilution that reduces survival of the pneumococci by at least 50%.

- It is important to note that the level of vaccine-induced pneumococcal antibody that correlates with protection against clinical disease has not been established in adults.

**CDC Summary of pivotal trials published in MMWR Report of "Licensure of 13-valent Pneumococcal Conjugate Vaccine for Adults Aged 50 years and Older".**

"In two randomized, multicenter, immunogenicity studies conducted in the United States and Europe, [pneumococcal-vaccine naïve] adults aged 50 years and older received a single dose of PCV13 or PPSV23. Functional antibody responses were measured 1 month after vaccination using an OPA assay. In adults aged 60 through 64 years, PCV13 elicited OPA geometric mean antibody titers (GMTs) to the 12 serotypes common to both vaccines that were comparable to, or higher than, responses elicited by PPSV23. For serotype 6A, which is unique to PCV13, OPA antibody responses were higher after PCV13 vaccination than after PPSV23 vaccination. OPA GMTs elicited by PCV13 in adults aged 50 through 59 years for all 13 serotypes were comparable to the corresponding GMTs elicited by administration of PCV13 in adults aged 60 through 64 years. In adults aged 70 years and older who previously had been immunized with a single dose of PPSV23 at least 5 years before enrollment, PCV13 elicited OPA responses that were comparable to or higher than those elicited by PPSV23 for the 13 serotypes. For 10 of 12 serotypes in common, the PCV13 responses were significantly greater than the PPSV23 responses. At 1-year follow up, OPA levels were lower in PCV13 and in PPSV23 recipients than at 1 month. An evaluation of responses after a second pneumococcal vaccination administered 1 year after the initial study doses showed that a second dose of PCV13 generally resulted in OPA levels similar to those observed after the first dose. In contrast, subjects who received PPSV23 as the initial study dose had lower OPA antibody responses after subsequent administration of PCV13 than those who had received PCV13 as the initial dose, regardless of the level of the initial OPA response to PPSV23."

Refer to Clinical Trials Details in Appendix Section

**Adverse Events (Safety Data)** [1]

Pooled safety data was derived from 6 clinical studies which included 6,198 adults (5,667 received PCV13) ranging in age from 50 through 95 years. Of the 5,667 PCV13 recipients, 3,751 adults had not previously received PPSV23 and 1,916 adults were previously vaccinated with PPSV23 at least 3 years prior to enrollment.

**Deaths and Other Serious Adverse Events** [1]

PCV13's package insert pooled serious adverse events and deaths across 6 clinical trials; no p-values or confidence intervals were provided. Overall, twelve of 5,667 (0.21%) PCV13 and four of 1,391 (0.28%) PPSV23 recipients died. All 12 of deaths who received PCV13 occurred between Day 3 and Day 309 post-vaccination. Two of these 12 deaths occurred within 30 days of vaccination with PCV13; both deaths were in subjects > 65 years of age (due to cardiac failure and peritonitis). The rates of pooled serious adverse event are listed in Table 3. There was a case of erythema multiforme that occurred 34 days following administration of a second dose of PCV13.

**Table 3. Serious Adverse Events**

| Incidence | PCV13 (n=5055) | PPSV23 (n=1124) |
|---|---|---|
| **Within 1 month post-vaccination** | 0.2% - 1.4% | 0.4% - 1.7% |
| **From 1 – 6 months post-vaccination** | 1.2% - 5.8% | 2.4% - 5.5% |

**Common Adverse Events** [1,3]

According to ACIP, similar adverse reactions were seen between PCV13 and PPSV23 in the clinical trials.

The commonly reported *local* adverse reactions after PCV13 vaccination were redness, swelling and pain at the injection site, or limitation of arm movement (refer to package insert Tables 9 and 10 for specific percentages and statistically more frequent occurrences).

The commonly reported *systemic* adverse reactions after PCV13 vaccination were fatigue, headache, chills, rash, decreased appetite, or muscle pain and joint pain (refer to package insert Tables 11 and 12 for specific percentages and statistically more frequent occurrences).

**Other Adverse Events**
There was an increase in mild injection reactions as well as, certain systemic reactions with the concomitant administration of PCV13 with influenza vaccine.

**Contraindications** [1]
PCV13 is contraindicated in patients with a severe allergic reaction (e.g., anaphylaxis) to any component of PCV13 or any diphtheria toxoid-containing vaccine.

**Warnings and Precautions (Adults)**[1]
- Epinephrine and other appropriate agents should be available immediately to manage allergic reactions.
- Data on the safety and effectiveness of PCV13 in the immunocompromised patients are unknown; these patients may have reduced antibody response due to impaired immune responsiveness.

**Special Populations (Adults)** [1]
**Pregnancy:** Pregnancy Category B

**Nursing:** It is not known whether this vaccine is excreted in human milk; thus, caution is advised when administered to a nursing woman.

**Geriatrics:** Lower antibody responses to PCV13 were observed in persons > 65 years of age compared to those in persons 50 through 59 years of age. No overall differences in safety outcomes were seen between these two groups.

**Immunocompromising Conditions:** Refer ACIP Recommendations in sections above.

**Postmarketing Safety Experience**
No data in adults.

**Sentinel Events**
No data in adults.

**Look-alike / Sound-alike (LA / SA) Error Risk Potential**
As part of a JCAHO standard, LASA names are assessed during the formulary selection of drugs. Based on clinical judgment and an evaluation of LASA information from three data sources (Lexi-Comp, First Databank, and ISMP Confused Drug Name List), the following drug names may cause LASA confusion:

| NME Drug Name | Lexi-Comp | First DataBank | ISMP | Clinical Judgment |
|---|---|---|---|---|
| **Pneumococcal 13-valent Conjugate Vaccine** | Pneumococcal 7-Valent Conjugate Vaccine<br><br>Pneumococcal 23-Valent Polysaccharide Vaccine | None | None | Pneumovax-23®<br><br>Meningococcal Vaccine |
| **Prevnar 13®** | None | None | None | Prevnar 7® |

## Drug Interactions[1]

### Drug-Drug Interactions

Individuals receiving immunosuppressive therapy such as irradiation, corticosteroids, antimetabolites, alkylating agents, and cytotoxic agents may have reduced immune response to PCV13.

### Concomitant Administration of Vaccines [1]

Please refer to the PCV13 package insert for concomitant administration in pediatrics.

In adults, the concomitant administration of PCV13 and influenza vaccine (Fluarix® for the 2007/2008 influenza season) was evaluated. Inferior influenza antibodies titers occurred during concomitant administration with PCV13 in the elderly for the A/H3N2 strain; inferior pneumococcal OPA titers occurred for some of the serotypes in adults when administered concomitantly with influenza vaccine (5 serotypes in ages 50-59 and 3 serotypes in ages ≥65). The clinical implications of these reduced immune responses when PCV13 and TIV are administered concomitantly are not known at this time.

## Acquisition Costs

Refer to VA pricing sources for updated information.

## Pharmacoeconomic Analysis [4]

The following is unpublished data provided in ACIP's PCV13 recommendations for use in adults with immunocompromising conditions: "A cost-effectiveness analysis was performed using a lifetime cohort model of an implemented vaccine program wherein persons with selected immunocompromising conditions were immunized with PCV13 at the time of diagnosis and then followed current PPSV23 vaccination guidelines starting 1 year later. PCV13 vaccine efficacy against IPD [invasive pneumococcal disease] and pneumonia (used as a proxy for effectiveness in the model) was 75% and 13%, respectively, for persons with HIV/AIDS and persons requiring dialysis, and 25% and 0%, respectively, for persons with hematologic cancer and for organ transplant recipients. Using the current costs of PCV13, PPSV23, and administration, the modeled program resulted in a cost saving of $7,600,000, added 1,360 quality-adjusted life years, and averted 57 cases of IPD (CDC, unpublished data, 2012). These savings accrued largely as a result of protection among patients on dialysis and those with HIV/AIDS. Heterogeneity across risk groups was driven by differences in pneumococcal serotypes causing disease and assumed vaccine efficacy in each subgroup. The model was sensitive to assumptions about vaccine efficacy, whereby increased estimation of PCV13 efficacy led to increases in cost-effectiveness."

## Conclusions

In adults 50 years of age and older, PCV13 is FDA approved for the prevention of pneumonia and invasive disease caused by *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. This indication is based on immunogenicity studies that evaluated antibody response of PCV13 compared to PPSV23. As part of the FDA accelerated approval process utilized for PCV13, the pharmaceutical company is currently conducting a clinical trial to evaluate the clinical benefit of PCV13 in persons who are pneumococcal-vaccine naïve. Due to the lack clinical outcomes data in adults coupled with unknown impact of routine vaccination with PCV13 in children on the serotypes causing pneumococcal disease in adults, ACIP is currently not recommending routine use of PCV13 in immunocompetent adults 50 years of age and older. However, due to the higher risk of pneumococcal disease in certain patient populations, ACIP is recommending the routine use of 13-valent pneumococcal conjugate vaccine for adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants. PCV13 should be administered to eligible adults in addition to the 23-valent pneumococcal polysaccharide vaccine.

## References

1. Prevnar 13® (Package Insert) 2011. Pfizer, Philadelphia, PA 19101, USA.
2. Pneumovax 23® (Package Insert) 2011. Merck & Co., Inc., Whitehouse Station, NJ 08889, USA.
3. Licensure of 13-valent pneumococcal conjugate vaccine for adults aged 50 years and older. MMWR. 2012 Jun;61(21):394-5.
4. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2012 Oct;61(40):816-9.
5. DeVore N, et al. Summary basis for regulatory action: Prevnar 13™ / pneumococcal 13-valent conjugate vaccine (Diphtheria CRM197 protein). Silver Spring (MD): Food and Drug Administration (US); 2011 Dec. 13 p. Report No.: BLA/STN 125324/262.
6. Clinicaltrials.gov (accessed Jan 13, 2012)

**Prepared 12/2012 by Shawn Depcinski, Pharm.D.; Contact: Melinda Neuhauser, Pharm.D., MPH**

## APPENDIX

<table>
<tr><td>Study Title</td><td>A Phase 3, Randomized, Active-Controlled, Modified Double-blind Trial Evaluating the Safety, Tolerability, and Immunogenicity of PCV13 Compared to PPSV23 in Adults Who Are Naive to PPSV23</td></tr>
<tr><td>Study Goals</td><td>Evaluate the immunogenicity, safety and tolerability of PCV13 compared to PPSV23 in adults who were pneumococcal-vaccine naïve</td></tr>
<tr><td>Methods</td><td>Study Design: Active-controlled, modified doubled blind (i.e., principal investigator and subject blinded but others not) clinical trial that randomized pneumococcal-naïve adults aged 60-64 years old to PCV13 or PPSV23. In addition, a second cohort of adults aged 50-59 years of age received one-dose of PCV13 in an open-label manner.<br>Primary efficacy endpoints:<br>- Antibody responses (serotype specific OPA GMTs) one month after vaccination.<br>- Percentage of participants achieving at least a 4-fold rise in OPA titer for serotype 6A one month after vaccination<br>Data Analysis:<br>- Noninferiority was defined as the lower limit of the 2-sided 95% CI for GMT ratio (PCV13/PPSV23) greater than 0.5<br>- For serotype 6A, statistically significantly greater response was defined as the lower limit of the 2-sided 95% CI for the GMT ratio (PCV13/PPSV23) greater than 2 (when PCV13 compared to PPSV23)</td></tr>
<tr><td>Criteria</td><td>Inclusion criteria<br>- Adults aged 50 to 64 years who were naïve to vaccination with PPSV23.<br>Exclusion criteria<br>- Previous immunization with any licensed or experimental pneumococcal vaccine.<br>- Serious chronic disorders including metastatic malignancy, severe chronic obstructive pulmonary disease (COPD) requiring supplemental oxygen, end stage renal disease with or without dialysis, clinically unstable cardiac disease, or any other disorder which in the investigator's opinion precludes the subject from participating in the study.<br>- Known or suspected impairment of immunological function.</td></tr>
<tr><td>Results</td><td>OPA GMTs in PPSV23-unvaccinated Adults Aged 50 through 59 Years Given PCV13; and in Adults Aged 60 through 64 Years Given PCV13 or PPSV23
<table>
<tr><td></td><td>PCV13</td><td>PCV13</td><td>PPSV23</td><td colspan="2">PCV13 50-59 yrs relative to 60-64 yrs</td><td colspan="2">PCV13 relative to PPSV23 to 60-64 yrs</td></tr>
<tr><td>Sero-type</td><td>50-59 yrs N=350-384 GMT</td><td>60-64 yrs N=359-404 GMT</td><td>60-64 yrs N=367-402 GMT</td><td>GMT Ratio</td><td>(95%CI)</td><td>GMT Ratio</td><td>(95%CI)</td></tr>
<tr><td>1</td><td>200</td><td>146</td><td>104</td><td>1.4</td><td>(1.08, 1.73)</td><td>1.4</td><td>(1.10, 1.78)</td></tr>
<tr><td>3</td><td>91</td><td>93</td><td>85</td><td>1.0</td><td>(0.81, 1.19)</td><td>1.1</td><td>(0.90, 1.32)</td></tr>
<tr><td>4</td><td>2833</td><td>2062</td><td>1295</td><td>1.4</td><td>(1.07, 1.77)</td><td>1.6</td><td>(1.19, 2.13)</td></tr>
<tr><td>5</td><td>269</td><td>199</td><td>162</td><td>1.4</td><td>(1.01, 1.80)</td><td>1.2</td><td>(0.93, 1.62)</td></tr>
<tr><td>6A</td><td>4328</td><td>2593</td><td>213</td><td>1.7</td><td>(1.30, 2.15)</td><td>12.1</td><td>(8.63, 17.08)</td></tr>
<tr><td>6B</td><td>3212</td><td>1984</td><td>788</td><td>1.6</td><td>(1.24, 2.12)</td><td>2.5</td><td>(1.82, 3.48)</td></tr>
<tr><td>7F</td><td>1520</td><td>1120</td><td>405</td><td>1.4</td><td>(1.03, 1.79)</td><td>2.8</td><td>(1.98, 3.87)</td></tr>
<tr><td>9V</td><td>1726</td><td>1164</td><td>407</td><td>1.5</td><td>(1.11, 1.98)</td><td>2.9</td><td>(2.00, 4.08)</td></tr>
<tr><td>14</td><td>957</td><td>612</td><td>692</td><td>1.6</td><td>(1.16, 2.12)</td><td>0.9</td><td>(0.64, 1.21)</td></tr>
<tr><td>18C</td><td>1939</td><td>1726</td><td>925</td><td>1.1</td><td>(0.86, 1.47)</td><td>1.9</td><td>(1.39, 2.51)</td></tr>
<tr><td>19A</td><td>956</td><td>682</td><td>352</td><td>1.4</td><td>(1.16, 1.69)</td><td>1.9</td><td>(1.56, 2.41)</td></tr>
<tr><td>19F</td><td>599</td><td>517</td><td>539</td><td>1.2</td><td>(0.87, 1.54)</td><td>1.0</td><td>(0.72, 1.28)</td></tr>
<tr><td>23F</td><td>494</td><td>375</td><td>72</td><td>1.3</td><td>(0.94, 1.84)</td><td>5.2</td><td>(3.67, 7.33)</td></tr>
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| | |
|---|---|
| | - In adults aged 60 through 64 years, 88.5% of persons who received PCV13 had a 4-fold increase in OPA titers for serotype 6a compared to 39.2% who received PPSV23 (statistically significant; p-value not provided). |
| **Conclusions** | - PCV13 is as immunogenic as PPSV23 for the 12 common serotypes contained in both vaccines;<br>- OPA GMTs for serotype 6A were statistically higher for adults who received PCV13 compared to PPSV23 |

| | |
|---|---|
| **Study Title** | A Phase 3, Randomized, Active-Controlled, Modified Double-Blind Trial, Evaluating the Safety, Tolerability And Immunogenicity of PCV13 compared to PPSV23 Vaccine in Ambulatory Elderly Individuals Aged 70 Years And Older Who Received One Dose of PPSV23 At Least 5 Years Prior To Study Enrollment |
| **Study Goals** | Evaluate the immunogenicity, safety and tolerability of PCV13 compared to PPSV23 in adults who previously received a dose of PPSV23 |
| **Methods** | **Study Design:** Active-controlled, modified doubled blind (i.e., principal investigator and subject blinded but others not) clinical trial that randomized adults aged 70 years and older to PCV13 or PPSV23.<br><br>**Primary efficacy endpoint:**<br>- Antibody responses (serotype specific OPA GMTs) one month after vaccination.<br>- Percentage of participants achieving at least a 4-fold rise in OPA titer for serotype 6A one month after vaccination<br>**Data Analysis:**<br>- Noninferiority was defined as the lower limit of the 2-sided 95% CI for GMT ratio (PCV/PPSV23) greater than 0.5<br>- For serotype 6A, statistically significantly greater response was defined as the lower limit of the 2-sided 95% CI for the GMT ratio (PCV13/PPSV23) greater than 2 (when PCV13 compared to PPSV23) |
| **Criteria** | **Inclusion criteria**<br>- Male or Female aged 70 years or older.<br>- Documented vaccination with 1 dose of PPSV23 at least 5 years previous.<br>- Healthy<br>**Exclusion criteria**<br>- Receipt of more than one dose of PPSV23 prior to enrollment<br>- History of severe adverse reaction to a vaccine<br>- Immunodeficiency |
| **Results** | OPA GMTs in PPSV23-Previously Vaccinated Adults Aged ≥ 70 Years Given PCV13 or PPSV23 |

| | | | PCV13 relative to PPSV23 | |
|---|---|---|---|---|
| Serotype | PCV13 N=400-426 GMT | PPSV23 N=395-445 GMT | GMT Ratio | (95% CI) |
| 1 | 81 | 55 | 1.5 | (1.17, 1.88) |
| 3 | 55 | 49 | 1.1 | (0.91, 1.35) |
| 4 | 545 | 203 | 2.7 | (1.93, 3.74) |
| 5 | 72 | 36 | 2.0 | (1.55, 2.63) |
| 6A | 903 | 94 | 9.6 | (7.00, 13.26) |
| 6B | 1261 | 417 | 3.0 | (2.21, 4.13) |
| 7F | 245 | 160f | 1.5 | (1.07, 2.18) |
| 9V | 181f | 90f | 2.0 | (1.36, 2.97) |
| 14 | 280 | 285 | 1.0 | (0.73, 1.33) |
| 18C | 907 | 481 | 1.9 | (1.42, 2.50) |

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<table>
<tr><td>19A</td><td>354</td><td>200</td><td>1.8</td><td>(1.43, 2.20)</td></tr>
<tr><td>19F</td><td>333</td><td>214</td><td>1.6</td><td>(1.17, 2.06)</td></tr>
<tr><td>23F</td><td>158</td><td>43</td><td>3.7</td><td>(2.69, 5.09)</td></tr>
</table>
- In adults 70 yrs and older, 71.1% of persons who received PCV13 had a 4-fold increase in OPA titer for serotype 6a compared to 27.3% who received PPSV23 (statistically significant; p-value not provided).
</td></tr>
<tr><td>Conclusions</td><td>- PCV13 is as immunogenic as PPSV23 for the 12 common serotypes contained in both vaccines;<br>- OPA GMTs for serotype 6A were statistically higher for adults who received PCV13 compared to PPSV23</td></tr>
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